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SERIAL NUMBER	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
07/841,617	02/25/92	NEUMEYER J	RBI-101XX

EXAMINER	
ZMURKO, M	

ART UNIT	PAPER NUMBER
2203	12

DATE MAILED: 10/21/92

WEINGARTEN, SCHURGIN,
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BOSTON, MA 02109

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☒ Responsive to communication filed on 10/6/92 ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), ~~_____~~ days from the data of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☒ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice re Patent Drawing, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, Form PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____

Part II SUMMARY OF ACTION

1. ☒ Claims 1-45 are pending in the application.
   Of the above, claims 13-24, 27-28, 37-45 are withdrawn from consideration.
2. ☐ Claims _____ have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 1-12, 25-26, and 29-36 are rejected.
5. ☐ Claims _____ are objected to.
6. ☒ Claims 1-12, 25-26, and 29-36 are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable. ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____ has (have) been ☐ approved by the examiner. ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed on _____, has been ☐ approved. ☐ disapproved (see explanation).
12. ☐ Acknowledgment is made of the claim for priority under U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

The elected species of the compound of claim 1 wherein:

R = a monofluoroalkyl group including ^{n}F where n=18 or 19,

R'= a C_nH_{2n+1} group where n=0 to 6,

X = an isotope of I, and

Y = H,

is acknowledged by the examiner. All other claims not dependent upon the genus compound originally claimed in claims 1 and 7 are withdrawn from further consideration.

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-12 and 29-36, drawn to a radiolabelled composition and a kit for its use, classified in Class 424, subclass 1.1.

II. Claims 25-26, drawn to a non-radiolabelled precursor, classified in Class 546, subclass 132.

The inventions are distinct, each from the other because of the following reasons:

Inventions of Group I and II are related as mutually exclusive species in intermediate-final product relationship. Distinctness is proven for claims in this relationship if the intermediate product is useful to make other than the final product (M.P.E.P. § 806.04(b), 3rd paragraph), and the species are patentably distinct (M.P.E.P. § 806.04(h)).

In the instant case, the intermediate product is deemed to be useful as a drug and the inventions are deemed patentably distinct

since there is nothing on this record to show them to be obvious variants. Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions anticipated by the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. § 103 of the other invention.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> "A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent."
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent."

The following is a quotation of 35 U.S.C. 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

Claims 1-12 and ~~24-25~~ 25-26 are rejected under 35 U.S.C. § 102 (a) as being clearly anticipated by Neumeyer et al.

Neumeyer et al. teach the development of radioligand probes suitable for PET and SPECT imaging. In the first full paragraph on page 3145, Neumeyer et al. state, "The affinities of Cocaine, alpha-CIT, beta-CIT, and beta-CFT for the dopamine and serotonin reuptake sites were determined from radioligand displacement studies using tissue homogenates prepared from baboon and rat brain." Neumeyer et al. conclude that [I-123]-beta-CIT is a useful SPECT probe of monoamine reuptake sites in primate brain. Neumeyer et al. also teach the synthesis of 2-carbomethoxy-3-beta-(4-iodophenyl)tropanes) from various precursors in Scheme 1.

Claims 1-12 are rejected under 35 U.S.C. § 102 (e) as being anticipated by Carroll et al.

Carroll et al. teach that tropane derivatives may be employed for imaging and other brain scanning techniques that allow the determination of the presence of cocaine receptors, such as neurotransmitters. In column 1, lines 16-30, Carroll et al. state, "... attempts to understand, diagnose, treat and prevent neural disorders rely, in part, on localization or imaging techniques, allowing researchers to determine the location, number, and size of specific neurological phenomena. Among those sites undergoing specific testing are cocaine receptors and dopamine transporter sites ... the compound must have a high affinity for the receptor in question ..." Carroll et al. continue by providing [H-3]WIN 35,428 as an example. Carroll et al. continue in column 2, by providing a family of compounds which have demonstrated a high affinity for binding to cocaine receptors, such as the dopamine transporters. Carroll et al. further teach the radiolabeling of these compounds with an iodo substituent.

Claims 1-12 and ~~24-25~~ 25-26 are rejected under 35 U.S.C. 103 as being unpatentable over Neumeyer et al., as mentioned above, in view of Jacobson et al.

Neumeyer et al. do not specifically teach the use of a monofluoroalkyl group including ^{n}F where n=18 or 19 for the R substituent claimed by applicant in his election of species. Jacobsen et al. teach that radioactive fluorine can be easily introduced into biologically active molecules containing amino groups. The compounds produced are useful in diagnostic nuclear medicine. Jacobson et al. state in column 1, lines 38-45, "It has been found that certain radiolabelled compounds will localize in the brain, heart, or in other target organs or tissues to a sufficient level to allow for imaging ... There has been increasing interest in finding compounds which will more effectively cross the blood-brain barrier ... Fluorine-18 is a positron emitting isotope which ... has been used extensively as a non-invasive in vivo tracer." It would be obvious to a person of ordinary skill in the art to fluorinate the alkyl group on the compound taught by Neumeyer et al. due to the radiolabelled fluorine to perform imaging and its similar electronegativity and size to hydrogen.

Claims 1-12 are rejected under 35 U.S.C. 103 as being unpatentable over Carroll et al., as mentioned above, in view of Jacobson et al.

Carroll et al. do not specifically teach the use of a monofluoroalkyl group including ^{n}F where n=18 or 19 for the R substituent claimed by applicant in his election of species. Jacobsen et al. teach that radioactive fluorine can be easily introduced into biologically active molecules containing amino groups. The compounds produced are useful in diagnostic nuclear medicine. Jacobson et al. state in column 1, lines 38-45, "It has been found that certain radiolabelled compounds will localize in the brain, heart, or in

other target organs or tissues to a sufficient level to allow for imaging ... There has been increasing interest in finding compounds which will more effectively cross the blood-brain barrier ... Fluorine-18 is a positron emitting isotope which ... has been used extensively as a non-invasive in vivo tracer." It would be obvious to a person of ordinary skill in the art to fluorinate the alkyl group on the compound taught by Carroll et al. due to the radiolabelled fluorine capability to perform imaging and its similar electronegativity and size to that of hydrogen.

Claims 29-36 are rejected under 35 U.S.C. 103 as being unpatentable over Carroll et al., as mentioned above, or Neumeyer et al., as mentioned above in view of Nosco.

Neither teaching specifically teaches a kit for preparation of the iodinated neuroprobe. The use of kits is widely acknowledged in the art of radiolabelling. Nosco teaches in column 2, lines 17-25, "... short half-life of radionuclides it is often nearly impossible to deliver the ready-to-use labelled product to the user. In such cases it is desirable to place the various reaction components at the user's disposal in a so-called kit. By means of the kit, the user himself can carry out the labelling reaction with the radionuclide in the clinical hospital ..." Thus to one of skill in the art it is clearly advantageous and obvious to use a kit when utilizing the radiolabelled compounds taught by Carroll et al. and Neumeyer et al.

The elected species was not found in the prior art.

An inquiry concerning this communication should be directed to Matthew Zmurko at telephone number (703) 308-3957.

Robert L. Stoll

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ART UNIT 223